

a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of T, M, and S, and a residue selected from the group consisting of Y at a carboxyl-terminal amino acid of the epitope; and, (ii) a second structural motif comprising a first amino acid residue at position three from an amino-terminal residue of the epitope, said first residue selected from the group consisting of D, E, A, and S, and a residue selected from the group consisting of Y at a carboxyl-terminal amino acid of the epitope,

wherein the immunogenic peptide induces a cytotoxic T cell response when in complex with an HLA-A1 molecule and is contacted with an HLA-A1-restricted cytotoxic T cell,

a molecule linked to said peptide to create a compound, with a *proviso* that neither the peptide, the molecule nor the compound comprise an entire native antigen; and,  
a human dose of pharmaceutically acceptable excipient.

7. The pharmaceutical composition of claim 6, wherein the peptide is isolated and purified from a protein in nature or synthesized to exactly correspond to a peptide sequence in nature.

8. The pharmaceutical composition of claim 6, wherein the composition comprises the peptide in a form of nucleic acids that encode the peptide.

9. The pharmaceutical composition of claim 8, wherein the composition comprises the peptide in a form of nucleic acids that encode the peptide and at least one additional peptide, with a *proviso* that neither an additional peptide nor a combination of the peptide and the at least one additional peptide is an entire native antigen.

10. The pharmaceutical composition of claim 6, wherein the composition comprises the peptide comprised by a longer peptide, with a *proviso* that the longer peptide is not an entire native antigen.

11. The composition of claim 6, wherein the peptide is derived from a cancer-associated antigen.
12. The composition of claim 11, wherein the peptide is derived from an antigen that is CEA.
13. The composition of claim 11, wherein the peptide is derived from an antigen that is HER2/neu.
14. The composition of claim 11, wherein the peptide is derived from an antigen that is p53.
15. The composition of claim 11, wherein the peptide is derived from an antigen that is a MAGE antigen.
16. The composition of claim 11, wherein the peptide is derived from an antigen that is a prostate antigen.
17. The composition of claim 6, wherein the peptide is derived from an antigen that is derived from a pathogenic agent.
18. The composition of claim 17, wherein the peptide is derived from an HIV antigen.
19. The composition of claim 17, wherein the peptide is derived from an HBV antigen.
20. The composition of claim 17, wherein the peptide is derived from an HCV antigen.

21. The composition of claim 17, wherein the peptide is derived from a malaria antigen.

22. The composition of claim 6, wherein the peptide comprised by the composition is immunogenic *in vitro* and/or *in vivo*.

23. The composition of claim 6, wherein the peptide binds to an HLA-A1 molecule at an  $IC_{50}$  less than about 500 nM.

24. The composition of claim 6, wherein the peptide induces a cytotoxic T cell response when complexed with an HLA-A1 molecule and is presented to an HLA-A1-restricted cytotoxic T cell.

25. The composition of claim 6, wherein the molecule is a lipid.

26. The composition of claim 6, wherein the molecule is a T helper epitope.

27. The composition of claim 26, wherein the molecule is a pan DR binding peptide.

28. The composition of claim 6, wherein the molecule is a cytotoxic T lymphocyte (CTL) epitope.

29. The composition of claim 6, wherein the molecule is the peptide.

30. The composition of claim 6, wherein the molecule is a carrier molecule.

31. A method for using a pharmaceutical peptide composition in accordance with claim 6, said method comprising:

providing a pharmaceutical composition of claim 6 which comprises an immunogenic peptide;

complexing a fragment of the immunogenic peptide, or the entire peptide if it consists of about 8-11 amino acids in length, with an HLA-A1 molecule, said fragment bearing the HLA-A1 motif; and,

contacting an HLA-A1-restricted CTL with the complex of the provided peptide and the HLA-A1 molecule, whereby a CTL response is induced.

32. A pharmaceutical composition comprising:

a therapeutically effective human dose of an immunogenic peptide that comprises an epitope consisting of about 8-11 amino acids, said epitope comprising a HLA-A1 structural motif selected from the group consisting of: (i) a first structural motif comprising a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of T, M, and S, and a residue selected from the group consisting of Y at a carboxyl-terminal amino acid of the epitope; and, (ii) a second structural motif comprising a first amino acid residue at position three from an amino-terminal residue of the epitope, said first residue selected from the group consisting of D, E, A, and S, and a residue selected from the group consisting of Y at a carboxyl-terminal amino acid of the epitope,

wherein the immunogenic peptide induces a cytotoxic T cell response when in complex with an HLA-A1 molecule and is contacted with an HLA-A1-restricted cytotoxic T cell,

with a *proviso* that the peptide does not comprise an entire native antigen; and, a human dose of pharmaceutically acceptable excipient.

33. The pharmaceutical composition of claim 32, wherein the peptide is isolated and purified from a protein in nature or synthesized to exactly correspond to a peptide sequence in nature.

34. The pharmaceutical composition of claim 32, wherein the composition comprises the peptide in a form of nucleic acids that encode the peptide.

35. The pharmaceutical composition of claim 34, wherein the composition comprises the peptide in a form of nucleic acids that encode the peptide and at least one additional peptide, with a *proviso* that neither an additional peptide nor a combination of the peptide and the at least one additional peptide is an entire native antigen.

36. The pharmaceutical composition of claim 32, wherein the composition comprises the peptide comprised by a longer peptide, with a *proviso* that the longer peptide is not an entire native antigen.

37. The composition of claim 32, wherein the peptide is derived from a cancer-associated antigen.

38. The composition of claim 37, wherein the peptide is derived from an antigen that is CEA.

39. The composition of claim 37, wherein the peptide is derived from an antigen that is HER2/neu.

40. The composition of claim 37, wherein the peptide is derived from an antigen that is p53.

41. The composition of claim 37, wherein the peptide is derived from an antigen that is a MAGE antigen.

42. The composition of claim 37, wherein the peptide is derived from an antigen that is a prostate antigen.

43. The composition of claim 32, wherein the peptide is derived from an antigen that is derived from a pathogenic agent.

44. The composition of claim 43, wherein the peptide is derived from an HIV antigen.

45. The composition of claim 43, wherein the peptide is derived from an HBV antigen.

46. The composition of claim 43, wherein the peptide is derived from an HCV antigen.

47. The composition of claim 43, wherein the peptide is derived from a malaria antigen.

48. The composition of claim 32, wherein the peptide comprised by the composition is immunogenic *in vitro* and/or *in vivo*.

49. A method for using a pharmaceutical peptide composition in accordance with claim 32, said method comprising:

providing a pharmaceutical composition of claim 32 which comprises an immunogenic peptide;

complexing a fragment of the immunogenic peptide, or the entire peptide if it consists of about 8-11 amino acids in length, with an HLA-A1 molecule, said fragment bearing the HLA-A1 motif; and,

contacting a CTL restricted by an HLA-A1 molecule with the complex of the provided peptide and the HLA-A1 molecule, whereby a CTL response is induced.

50. An immunogenic composition, said composition comprising:  
an immunogenic peptide that comprises an epitope consisting of about 8-11 amino acids, said epitope comprising an HLA-A1 structural motif selected from the group consisting of: (i) a first structural motif comprising a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of T, M, and S, and a residue selected from the group consisting of Y at a carboxyl-terminal amino acid of the epitope; and, (ii) a second structural motif comprising a first amino acid residue at position three from an amino-terminal residue of the epitope, said first residue selected from the group consisting of D, E, A, and S, and a residue selected from the group consisting of Y at a carboxyl-terminal amino acid of the epitope; and,  
a molecule linked to said peptide to create a compound, with a *proviso* that neither the peptide, the molecule nor the compound comprise an entire native antigen.

51. The peptide of claim 50, wherein the peptide is in a form of nucleic acids that encode the peptide.

52. The peptide of claim 50, wherein the peptide is in a form of nucleic acids that encode the peptide and at least one additional peptide, with a *proviso* that neither an additional peptide nor a combination of the peptide and the at least one additional peptide is an entire native antigen.

53. The peptide of claim 50, wherein the peptide is comprised by a longer peptide, with a *proviso* that the longer peptide is not an entire native antigen.

54. A pharmaceutical composition comprising a peptide sequence of claim 50 and a pharmaceutically acceptable excipient.

55. The composition of claim 54, wherein the peptide is in a therapeutically effective human dose, and the pharmaceutically acceptable excipient is in a human dose.

56. The peptide of claim 50, wherein the peptide is immunogenic *in vitro* and/or *in vivo*.
57. The peptide of claim 50 wherein the peptide binds to an HLA-A1 molecule at an  $IC_{50}$  less than about 500 nM.
58. The peptide of claim 50, wherein the peptide induces a cytotoxic T cell response when complexed with an HLA-A1 molecule and is presented to an HLA-A1-restricted cytotoxic T cell.
59. The composition of claim 50, wherein the molecule is a lipid.
60. The composition of claim 50, wherein the molecule is a T helper epitope.
61. The composition of claim 60, wherein the molecule is a pan DR binding peptide.
62. The composition of claim 50, wherein the molecule is a cytotoxic T lymphocyte (CTL) epitope.
63. The composition of claim 50, wherein the molecule is the peptide.
64. The composition of claim 50, wherein the molecule is a carrier molecule.



65. A pharmaceutical composition comprising:

a therapeutically effective human dose of an immunogenic peptide that comprises an epitope consisting of about 8-11 amino acids, said epitope comprising an HLA-A3 structural motif comprising a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of L, M, V, I, S, A, T, F, C, G, and D, and a residue selected from the group consisting of K, Y, R, H, and, F at a carboxyl-terminal amino acid of the epitope;

wherein the immunogenic peptide induces a cytotoxic T cell response when in complex with an HLA-A3 molecule and is contacted with an HLA-A3-restricted cytotoxic T cell,

a molecule linked to said peptide to create a compound, with a *proviso* that neither the peptide, the molecule nor the compound comprise an entire native antigen; and, a human dose of pharmaceutically acceptable excipient.

66. A pharmaceutical composition comprising:

a therapeutically effective human dose of an immunogenic peptide that comprises an epitope consisting of about 8-11 amino acids, said epitope comprising an HLA-A3 structural motif comprising a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of L, M, V, I, S, A, T, F, C, G, and D, and a residue selected from the group consisting of K, Y, R, H, and, F at a carboxyl-terminal amino acid of the epitope;

wherein the immunogenic peptide induces a cytotoxic T cell response when in complex with an HLA-A3 molecule and is contacted with an HLA-A3-restricted cytotoxic T cell,

with a *proviso* that the peptide does not comprise an entire native antigen; and, a human dose of pharmaceutically acceptable excipient.

67. An immunogenic composition, said composition comprising:  
an immunogenic peptide that comprises an epitope consisting of about 8-11 amino acids, said epitope comprising an HLA-A3 structural motif comprising a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of L, M, V, I, S, A, T, F, C, G, and D, and a residue selected from the group consisting of K, Y, R, H, and F at a carboxyl-terminal amino acid of the epitope; and,

a molecule linked to said peptide to create a compound, with a *proviso* that neither the peptide, the molecule nor the compound comprise an entire native antigen.

68. A pharmaceutical composition comprising:  
a therapeutically effective human dose of an immunogenic peptide that comprises an epitope consisting of about 8-11 amino acids, said epitope comprising an HLA-A11 structural motif comprising a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of L, M, I, V, A, S, T, G, N, C, F, and D, and a residue selected from the group consisting of K, R, and H, at a carboxyl-terminal amino acid of the epitope;

wherein the immunogenic peptide induces a cytotoxic T cell response when in complex with an HLA-A11 molecule and is contacted with an HLA-A11-restricted cytotoxic T cell,

a molecule linked to said peptide to create a compound, with a *proviso* that neither the peptide, the molecule nor the compound comprise an entire native antigen; and,

a human dose of pharmaceutically acceptable excipient.

69. A pharmaceutical composition comprising:

a therapeutically effective human dose of an immunogenic peptide that comprises an epitope consisting of about 8-11 amino acids, said epitope comprising an HLA-A11 structural motif comprising a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of L, M, I, V, A, S, T, G, N, C, F, and D, and a residue selected from the group consisting of K, R, and H, at a carboxyl-terminal amino acid of the epitope;

wherein the immunogenic peptide induces a cytotoxic T cell response when in complex with an HLA-A11 molecule and is contacted with an HLA-A11-restricted cytotoxic T cell,

with a *proviso* that the peptide does not comprise an entire native antigen; and,  
a human dose of pharmaceutically acceptable excipient.

70. An immunogenic composition, said composition comprising:

an immunogenic peptide that comprises an epitope consisting of about 8-11 amino acids, said epitope comprising an HLA-A11 structural motif comprising a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of L, M, I, V, A, S, T, G, N, C, F, and D, and a residue selected from the group consisting of K, R, and H, at a carboxyl-terminal amino acid of the epitope; and,

a molecule linked to said peptide to create a compound, with a *proviso* that neither the peptide, the molecule nor the compound comprise an entire native antigen.

71. A pharmaceutical composition comprising:

a therapeutically effective human dose of an immunogenic peptide that comprises an epitope consisting of about 8-11 amino acids, said epitope comprising an HLA-A24.1 structural motif comprising a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of Y, F, and W, and a residue selected from the group consisting of F, I, L, and W, at a carboxyl-terminal amino acid of the epitope;

wherein the immunogenic peptide induces a cytotoxic T cell response when in complex with an HLA-A24.1 molecule and is contacted with an HLA-A24.1-restricted cytotoxic T cell,

a molecule linked to said peptide to create a compound, with a *proviso* that neither the peptide, the molecule nor the compound comprise an entire native antigen; and,  
a human dose of pharmaceutically acceptable excipient.

72. A pharmaceutical composition comprising:

a therapeutically effective human dose of an immunogenic peptide that comprises an epitope consisting of about 8-11 amino acids, said epitope comprising an HLA-A24.1 structural motif comprising a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of Y, F, and W, and a residue selected from the group consisting of F, I, L, and W, at a carboxyl-terminal amino acid of the epitope;

wherein the immunogenic peptide induces a cytotoxic T cell response when in complex with an HLA-A24.1 molecule and is contacted with an HLA-A24.1-restricted cytotoxic T cell,

with a *proviso* that the peptide does not comprise an entire native antigen; and,  
a human dose of pharmaceutically acceptable excipient.

73. An immunogenic composition, said composition comprising:  
an immunogenic peptide that comprises an epitope consisting of about 8-11 amino acids, said epitope comprising an HLA-A24.1 structural motif comprising a first amino acid residue at position two from an amino-terminal residue of the epitope, said first residue selected from the group consisting of Y, F, and W, and a residue selected from the group consisting of F, I, L, and W, at a carboxyl-terminal amino acid of the epitope; and,  
a molecule linked to said peptide to create a compound, with a *proviso* that neither the peptide, the molecule nor the compound comprise an entire native antigen.--

REMARKS

With this amendment, Applicants request entry of new claims 6-73 in the patent application. These claims replace originally filed claims 1-5. Applicants thank the Examiner for the interview with Applicants' attorneys, Ellen Weber and Timothy J. Lithgow, on July 21, 1999 in which this case was discussed. The newly added claims are being submitted as discussed in the interview.

Support for the new claims can be found throughout both the present application and related applications U.S.S.N. 08/159,339, 08/821,739 and 08/186,266, which are incorporated by reference. Once allowable claims are indicated and if requested, Applicants will physically incorporate text from the related application into this application.

Claims 6, 24, 32, 50, 58, 65, 66, 68, 69, 71, and 72 recite a composition that induces an HLA-restricted cytotoxic T lymphocyte ("CTL") response. These claims add no new matter. Support for this amendment can be found, e.g., in the specification on page 111, line 19 through page 12, line 19.

Claims 6, 32, 55, 65, 66, 68, 69, 71, and 72 have been amended to recite a therapeutically effective dose and a pharmaceutical excipient. These claims add no new matter. Support for these claims can be found, e.g., in the specification on page 19, lines 28-31 and page 21, lines 7-23.

Claims 7 and 33 have been amended to recite peptide synthesized or isolated from naturally occurring sources. This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 12, line 21.